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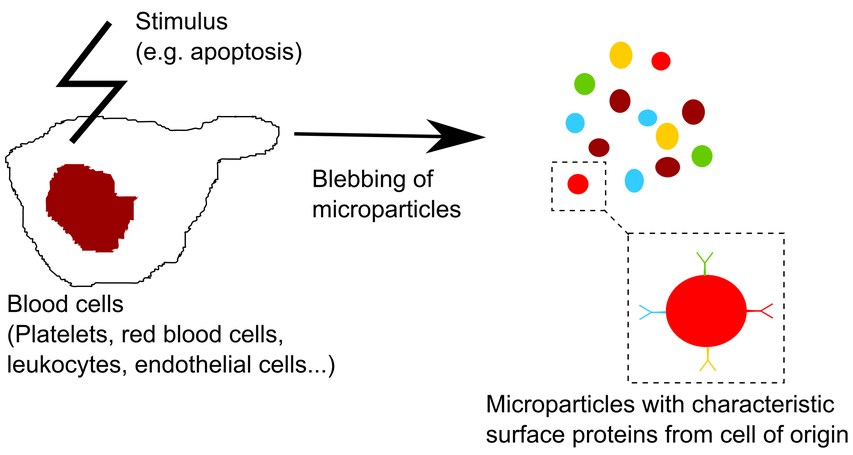
Towards a diffusion-based microfluidic device for the isolation of cell-derived microparticles

Solène Cherré[1]*, Mark Holm Olsen[1], Noemi Rozlosnik[1]
[1]Department of Micro- and Nanotechnology, Technical University of Denmark, Kongens Lyngby, Denmark

Introduction

Cell-derived microparticles (MPs) have been proposed as novel diagnostics markers for a wide range of diseases such as autoimmune diseases and cancer. They are small vesicles (size range: 50 nm to 1 µm) shed by all types of cells and circulating in the blood. Owing the small size and the complex environment of blood, purification of MPs remains challenging and lacks standardization in order to obtain reliable and comparable analysis data [1,2]. In this work, we present the theoretical development and implementation of a diffusion-based sorting microfluidic device for the purification of MPs.



Modeling

The aim of our device was to separate immuncomplexes and other smaller vesicles from MPs samples by diffusion. The diffusion coefficient, dependent of the size of the particles, is larger for small particles, so that they migrate faster along a concentration gradient compared to larger particles [3]. Figure 3 shows the setup of our device, where a buffer stream and a sample stream are flown from two inlets in a laminar regime (Re <<1). We used a finite element simulation in order to predict the concentration of five representative types of particles or molecules at both outlets (Figure 1).

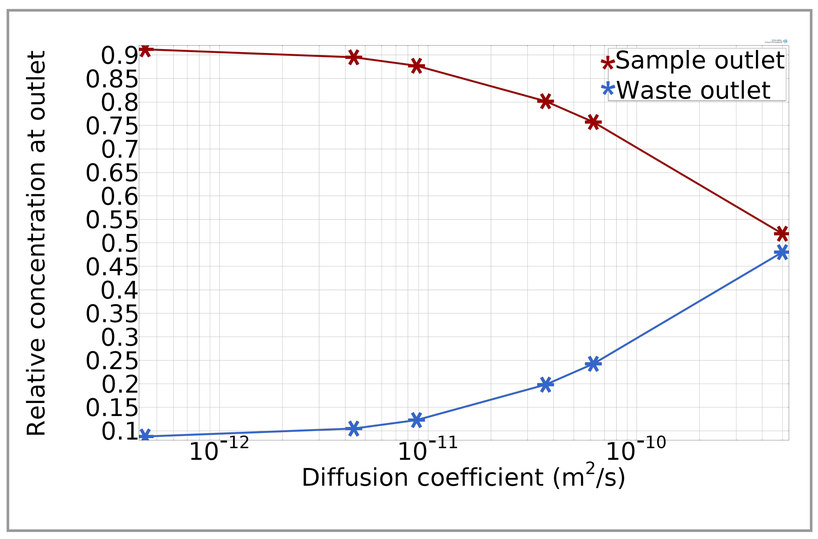


Figure 1: Relative concentration at the sample and the waste outlet for 5 representative particles and molecules

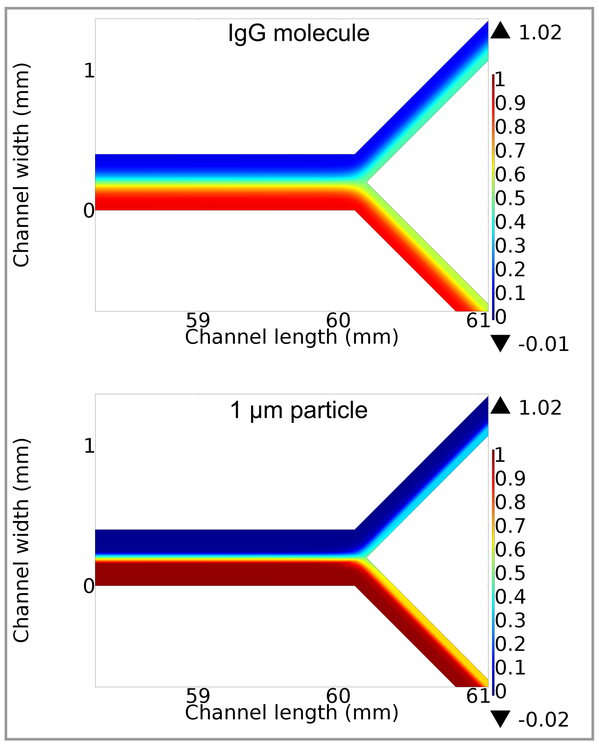


Figure 2: Concentration profile of two samples at the outlets of the channel

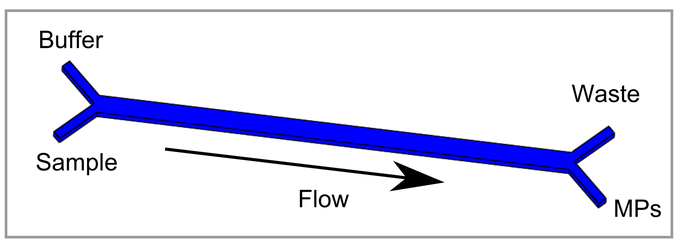


Figure 3: Setup of the diffusion-based sorting device

Experimental work

The device was fabricated in the polymer PMMA (Poly(methyl methacrylate)) using micromilling and thermobonding. Figure 4 shows a picture of the device at the intersection between the central channel and the inlets channels. Four different samples were flown through the chanel with a flow rate of 2.5 µl/min. The concentration was measured before and after the channel in both outlets. Figure 5 shows the concentrations at both outlets relative to the initial concentration introduced at the sample inlet.
The larger samples (1 µm and 100 nm particles) were completely collected in the sample outlet as the convection time over the length of the channel was shorter than the diffusion time over the half width of the channel. In contrast, smaller samples such as the antibody IgG diffused to the waste channel. The sample was therefore purified from 50% of the antibody IgG.

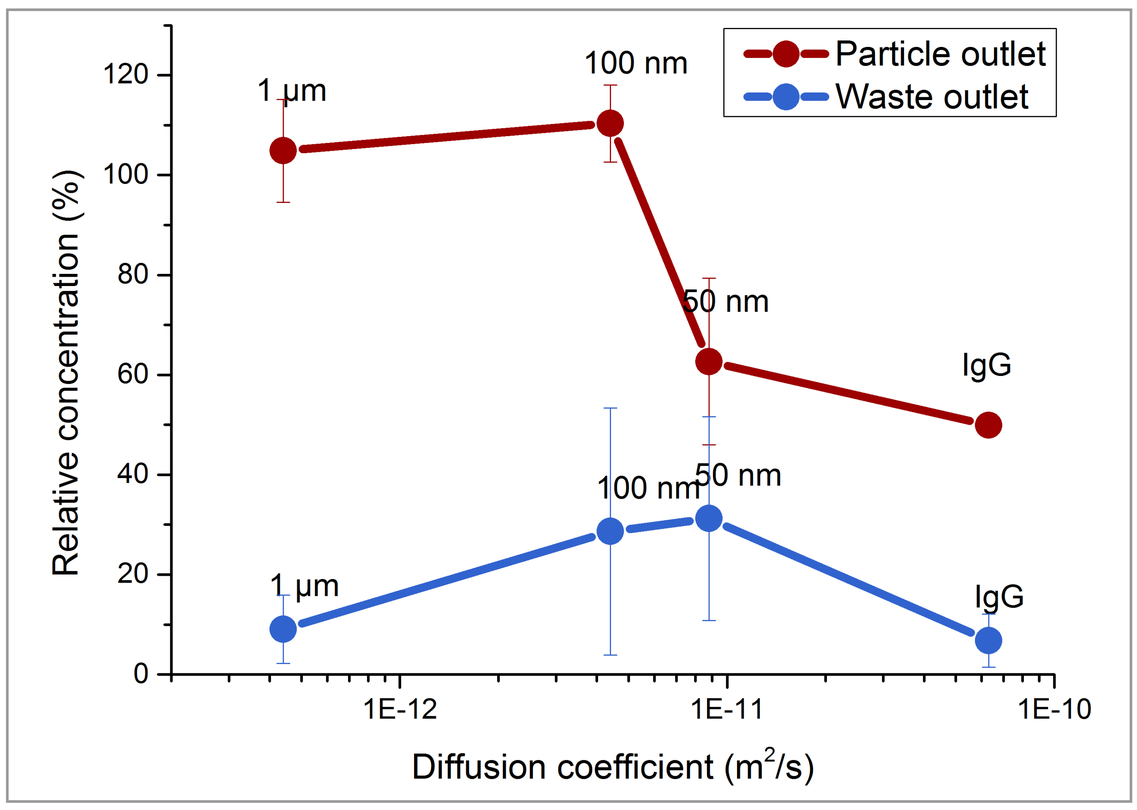


Figure 5: Relative concentration of 4 samples at both outlets of the device. n = 3

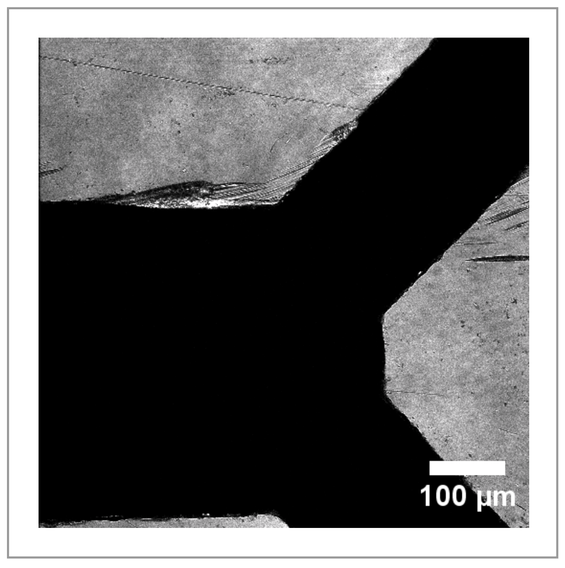


Figure 4: Image of the channel at the inlet. The image was obtained using a confocal microscope. The size of the central channel was 400 µm, while the side channels were 200 µm wide.
The depth of the central channel was 270 µm.

Conclusion and outlook

In this work we show the development of a microfluidic system , where MPs can be purified from plasma sample through diffusion. To increase the separation efficiency, the samples will go through several steps of purification.
This technique has the potential to become a powerful tool to isolate MPs from complex enviroments.

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* solch@nanotech.dtu.dk